NON-TECHNICAL ABSTRACT

Autologous transplantation is a technique which makes safe the very high doses of chemotherapy which are required to eradicate some populations of breast cancer cells. Although the responses seen in poor prognosis breast cancer patients is often dramatic following the intensive therapy used in autologous transplantation, most patients who respond do not exhibit increased survival. This indicates that additional therapy following recovery from the transplant might be beneficial. In order to make possible the delivery of relatively intensive doses of taxol following autologous transplant, we will introduce the MDR-1 cDNA into the stem cells of patients with breast cancer before storage for transplant. The peripheral blood stem cells for transduction is removed from the patient at the time of remission induced by conventional dose chemotherapy, stored and re-infused into the patient after intensive therapy in order to restore marrow function. To accomplish this, 50% of the peripheral blood cells stored from breast cancer patients will be incubated with the multidrug resistance (pVMDR-1) chemotherapy resistance vector. This vector will introduce a MDR-1 cDNA into the peripheral blood cells. The establishment of this gene in the cells will promote their growth over unmodified cells following taxol chemotherapy given following the autograft. If this is the case, we will be in a position to safely deliver high dose taxol after autologous transplant in breast cancer patients and thereby alter the unfavorable natural history of this disease. The results of this study will be used to improve the therapy given to patients with breast cancer. It is not designed to benefit the patients themselves.